COVID-19 vaccination elicits an evolving, cross-reactive antibody response to epitopes conserved with endemic coronavirus spike proteins.

Journal: Cell Rep

Publication Year: 2022

Authors: Evan A Elko, Georgia A Nelson, Heather L Mead, Erin J Kelley, Sophia T Carvalho, Nathan G Sarbo, Caroline E Harms, Virginia Le Verche, Angelo A Cardoso, Jennifer L Ely, Annalee S Boyle, Alejandra Pina, Sierra N Henson, Fatima Rahee, Paul S Keim, Kimberly R Celona, Jinhee Yi, Erik W Settles, Daniela A Bota, George C Yu, Sheldon R Morris, John A Zaia, Jason T Ladner, John A Altin

PubMed link: 35753310

Funding Grants: Evaluation and Characterization of SARS-CoV-2 Antibody in Convalescent Volunteer Plasma Donors for Potential Therapeutic Use

Public Summary:
The COVID-19 pandemic has triggered the first widespread vaccination campaign against a coronavirus (CoV). Many vaccinated subjects were previously infected with other coronaviruses (CoVs), and this study asked whether this prior coronavirus immunity influences the vaccine response. Here, we used blood samples from vaccinated persons and others to identify the Moderna mRNA-1273 vaccine could induce antibody responses against a range of CoV proteins. The testing used proteins that were either common to many CoV's or not common. We observed distinct differences in immune responses to the common CoV proteins from the surface of the CoV: these become detectable sooner and decayed at later time points after vaccination than other virus proteins. In addition, we showed that these distinct immune responses reflected an evolving cross-reactive response that can distinguish important proteins, and these results could reveal mechanisms for the formation of antibodies with broad reactivity against other CoVs. This finding could become useful in future vaccine development.

Scientific Abstract:
The COVID-19 pandemic has triggered the first widespread vaccination campaign against a coronavirus. Many vaccinated subjects are previously naive to SARS-CoV-2; however, almost all have previously encountered other coronaviruses (CoVs), and the role of this immunity in shaping the vaccine response remains uncharacterized. Here, we use longitudinal samples and highly multiplexed serology to identify mRNA-1273 vaccine-induced antibody responses against a range of CoV Spike epitopes, in both phylogenetically conserved and non-conserved regions. Whereas reactivity to SARS-CoV-2 epitopes shows a delayed but progressive increase following vaccination, we observe distinct kinetics for the endemic CoV homologs at conserved sites in Spike S2: these become detectable sooner and decay at later time points. Using homolog-specific antibody depletion and alanine-substitution experiments, we show that these distinct trajectories reflect an evolving cross-reactive response that can distinguish rare, polymorphic residues within these epitopes. Our results reveal mechanisms for the formation of antibodies with broad reactivity against CoVs.